Remarks

The claims are 1-14. Claims 1 and 13 have been amended to recite a mixture of hydrophilic and lipophilic solvents that, at the highest amount of hydrophilic content, is about 65:35. Support for this recitation can be found in the original specification at, for example, page 2, line 3. Accordingly, the changes are not new matter.

I. Rejections Over U.S. Patent No. 5,792,469

Claims 1-14 have been rejected under 35 U.S.C. § 103 as allegedly being unpatentable over U.S. Patent No. 5,792,469 ("Tipton"). Applicants respectfully submit that Tipton does not make obvious the present invention as claimed in Claims 1 and 13, as amended. Tipton discloses ten Examples of his invention. In none of the Tipton Examples is there disclosure of a mixture of hydrophilic and lipophilic solvents that is about 65:35 **or less of the hydrophilic solvent**.

EXAMPLE 1 of Tipton discloses a (1) mixture of about 5% of an equimolar mixture of sodium carbonate and citric acid, (2) about 60% N-methyl pyrrolidone, and (3) about 3.5% of a 50/50 copolymer of poly(di-lactide) and polycaprolactone. The sum of the percentages do not add to 100. Normalizing to 100 shows that the disclosed mixture is 87.6% N-methyl pyrrolidone ("NMP", an hydrophilic solvent). Thus, even if the other components were lipophilic, the ratio of hydrophilic to lipophilic is **at least** 87.6:12.3. Thus, EXAMPLE 1 teaches a ratio of hydrophilic to lipophilic that is outside the range of Claims 1 and 13, as amended.

What is normalized?

Similarly, EXAMPLE 2, normalized to 100 yields a percentage of NMP of 94.4%. EXAMPLE 3 normalized to 100 of the two disclosed mixtures yields NMP percentages of 89.5% and 94.7%. EXAMPLE 4, sums to 100, and yields an NMP percentage of 90%. EXAMPLE 5, normalized to 100, yields an NMP percentage of 94.7%. EXAMPLE 6, normalized to 100, yields an NMP percentage of 94.4%. EXAMPLE 7, sums to 100, and yields an NMP percentage of 89%. EXAMPLE 8, sums to 100, and yields an NMP percentage of 90%. EXAMPLE 9, **sums to 101**, and yields an NMP percentage of 82.2%. EXAMPLE 10, **sums to 105**, and yields an NMP percentage of 92.8%.

The Tipton examples use NMP at percentages of 87.6, 94.4, 89.5, 94.7, 90, 94.7, 94.7, 89, 90, 82.2, and 90. Thus, **in all cases**, Tipton utilizes a hydrophilic component that is at least 82.2% - well above the 65% or less embraced by independent Claims 1 and 13, as amended. In

no instance does Tipton disclose the range of hydrophilic:lipophilic solvents of from about 65:35 to about 0:100.

Tipton discloses only one formulation that was placed subcutaneously – and that example (EXAMPLE 1) utilized a high NMP percentage of 87.6%. Tipton is silent in regard to the important element of at least 35% lipophilic solvent in the solvent system as recited in the present independent Claims 1 and 13.

Thus, Tipton does not suggest, motivate, or teach the film coated liquid implant formed by a method comprising injecting into a subject in need of said implant at an implant site a liquid polymeric composition for controlled release of hydrophobic bioactive substances comprising: (a) 1 to 30% w/v of a hydrophobic bioactive substance; (b) 1 to 20% w/v of a poly(lactide-co-glycolide) copolymer; wherein the weight ratio of the poly(lactide-co-glycolide) copolymer to the hydrophobic bioactive substance is 1:1 or less; and (c) a mixture of hydrophilic and lipophilic solvents is from about 65:35 to about 5:95; wherein said composition is effective to form said film coated liquid implant at said implant site.

And Tipton does not suggest, motivate, or teach the film coated liquid implant formed by a method comprising injecting into a subject in need of said implant at an implant site a liquid polymeric composition comprising (a) about 1-30% w/v of at least one bioactive substance; (b) about 1-20% w/v of at least one biologically acceptable polymer, wherein the weight ratio of the polymer to the bioactive substance is 1:1 or less; and (c) at least one lipophilic solvent or a mixture of at least one hydrophilic solvent and at lest one lipophilic solvent, wherein the volume ratio of the hydrophilic and lipophilic solvents is from about 65:35 to about 0:100, and/or wherein the lipophilic solvent is present in an amount of at least about 16.5% by weight; wherein said composition is effective to form a film coated liquid at said implant site.

Therefore, independent claims 1 and 13 are not obvious over Tipton. Claims 2-12, and 14 depending from claims 1 and 13 respectively are also not obvious for that reason as well as for the additional elements they contain. Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

Conclusion

Applicants respectfully submit that the application is in condition for allowance and request a Notice to that effect. If a telephonic discussion would be helpful to further the prosecution, Applicants' attorney can be reached at the telephone number below.

Correspondence should continue to be directed to the address below. Any deficiencies in fees should be charged to Deposit Account **13-2755**.

EXPRESS MAIL CERTIFICATE
DATE OF DEPOSIT 12/13/2001
EXPRESS MAIL NO. EL992076396US
I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS EXPRESS MAIL "POST OFFICE TO ADDRESSEE" BEFORE 5 P.M. ON THE ABOVE DATE IN AN ENVELOPE ADDRESSED TO ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231
MAILED BY JB Crowley
DATE 12/13/01

Date: December 13, 2001

Respectfully submitted,

By Shu M. Lee

Shu M. Lee
Reg. No. 41,147
Attorney for Applicants

MERCK & CO., Inc.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-2675